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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,055	06/20/2003	Uwe Ries	01-1358	5854
28501 7590 03/31/2008				
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EXAMINER				
WANG, SHENGJUN				
ART UNIT		PAPER NUMBER		
1617				
MAIL DATE		DELIVERY MODE		
03/31/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/600,055

Applicant(s)

RIES ET AL.

Examiner

Shengjun Wang

Art Unit

1617

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3-11 and 13-19 is/are pending in the application.
- 4a) Of the above claim(s) 7-10, 13-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-6 and 11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted December 27, 2007 is acknowledged.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 1, 3-6, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ries et al. (WO00/01704, or 6,248,770 as English equivalent, IDS), in view of Romisch et al. (EP 1 027 894), Tsukada et al. (EP 0 781 558) and Iqbal et al. and in further view of Merck Manual regarding bacteraemia.

2. Ries et al. teaches that the compounds herein, including their stereoisomers, are known as antithrombotic pharmaceutical agents. The elected compound 2-(4-amidinophenylaminomethyl)-1-methyl-5-[1-(carboxymethylamino)-1-(pyrro lidin-1-yl-carbonyl)-ethyl]-benzimidazole is one of the preferred compounds. See, particularly, the abstract, the examples, and the claims. As racemics, the compounds may be separated into enantiomers by conventional method. The compounds may be used in the forms of any pharmaceutical acceptable salts, including salt with hydrochloric acid. See col. 19, line 45 to col. 20, line 15 in '770.

3. Ries et al. do not teach expressly the employment of the particular antithrombotic agent for treating sepsis, or related disorders, bacteraemia.

However, Romisch et al. Tsukada et al. and Iqbal et al. disclosed that antithrombotic agents (such as antithrombins) have been known as useful for treatment of sepsis. See, particularly, the abstracts and the claims of both Tsukada et al. and Romisch et al. and the abstract of Iqbal et al. Sepsis, is an stage of Systemic inflammatory responsive syndrome, and often arise from bacteraemia (Merck Manual). Microvascular thrombosis and disseminated intravascular coagulation are the common symptoms for sepsis. See, columns 1-2 in Romisch et al. and pages 111-115 of Iqbal et al. It is also known in the art that anticoagulants agent, including those of antithrombotic agents are expected to be useful for treating sepsis. See, page 118 and 119 in Iqbal et al.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ the compound herein for the treatment or prophylactic treatment of sepsis, including for those patients suffering from bacteraemia. The employment of the particular compound as the antithrombotic agent is obvious as it is disclosed as one of the preferred compounds. The employment of the particular enantiomer in the particular salt form would have been obvious since Reis teaches that all the enantiomer and pharmaceutical acceptable salts are similarly useful.

4. A person of ordinary skill in the art would have been motivated to employ the compounds herein for the treatment or prophylactic treatment of sepsis, including for those patients suffering from bacteraemia because antithrombotic agents are known to be useful for treatment of sepsis. The employment of the particular compound as the antithrombotic agent is

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obvious as it is disclosed as one of the preferred compounds. The employment of the particular enantiomer in the particular salt form would have been obvious since Reis teaches that all the enantiomer and pharmaceutical acceptable salts are similarly useful. Furthermore, one of the ordinary skill would have found it obvious to employ a stereoisomer of the known antithrombotic compounds herein in the claimed method since it is considered within the skill of the art to resolve the optical isomers of a known chiral compound, and each isomer is expected to be active in the absence of evidence to the contrary. See In re Anthony 162 USPQ 594; In re Adamson 125 USPQ 233.

Finally, the further employment of another antithrombotic agents, such as antithrombin, would have been obvious to one of ordinary skill in the art, because it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus , the claimed invention which drawn to the employment of a combination of two known antithrombotic agents sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069.

Response to the Arguments

Applicants' amendments and remarks submitted December 27, 2007 have been fully considered, but are not persuasive.

Applicants again assert that Romisch et al. (EP 1 027 894), Tsukada et al. (EP 0 781 558) and Iqbal et al. teach away from the claimed invention because each of the references teaches antithrombotic agents with different biological mechanisms. The arguments are not persuasive.

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Particularly, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). The references as a whole have clearly suggested that antithrombotic agents are useful for treatment of sepsis regardless of the biochemical mechanism. Furthermore, the prior art need not suggest combining references for the same reason that a patent applicant combined them. See *KSRInt'l Co. v. TeleflexInc.*, 127 S.Ct. 1727, 1741-42 (2007) ("In determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. *. [A]ny need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed."). *Romisch et al.* (EP 1 027 894), *Tsukada et al.* (EP 0 781 558) and *Iqbal et al.* may not teach expressly the particular functions of antithrombotic agents as applicants' asserted, the references as a whole do suggest the usefulness of antithrombotic agents for treatment of sepsis.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617